General

Guideline Title

Apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation.

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation. London (UK): National Institute for Health and Clinical Excellence (NICE); 2013 Feb. 44 p. (Technology appraisal guidance; no. 275).

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Apixaban is recommended as an option for preventing stroke and systemic embolism within its marketing authorisation, that is, in people with nonvalvular atrial fibrillation with 1 or more risk factors such as:

- Prior stroke or transient ischaemic attack
- Age 75 years or older
- Hypertension
- Diabetes mellitus
- Symptomatic heart failure

The decision about whether to start treatment with apixaban should be made after an informed discussion between the clinician and the person about the risks and benefits of apixaban compared with warfarin, dabigatran etexilate and rivaroxaban. For people who are taking warfarin, the potential risks and benefits of switching to apixaban should be considered in light of their level of international normalised ratio (INR) control.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Stroke
- Systemic embolism
- Nonvalvular atrial fibrillation

Guideline Category

Assessment of Therapeutic Effectiveness

Prevention

Clinical Specialty

Cardiology

Family Practice

Geriatrics

Hematology

Internal Medicine

Neurology

Preventive Medicine

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To assess the clinical effectiveness and cost-effectiveness of apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation

Target Population

Adult patients with nonvalvular atrial fibrillation, with 1 or more risk factors, such as prior stroke or transient ischaemic attack, age 75 years or older, hypertension, diabetes mellitus, or symptomatic heart failure (New York Heart Association [NYHA] class 2 or higher)

Interventions and Practices Considered

Apixaban

Major Outcomes Considered

- Clinical effectiveness
  - Stroke
  - Systemic embolism
  - Myocardial infarction (fatal and non-fatal)
  - Composite outcomes (e.g., all strokes, myocardial infarction or vascular death)
  - Major/minor bleeding
  - Intracranial bleeding
  - Gastrointestinal bleeding
  - Hepatic safety
  - Mortality
  - Re-admission rates
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The Evidence Review Group (ERG) report for this technology appraisal was prepared by Biomedical Journals Technology Assessment Group (BMJ-TAG) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

The manufacturer conducted two systematic reviews (SRs) to identify published reports of trials relevant to the decision problem that is the focus of this single technology appraisal (STA).

Description and Critique of Manufacturer's Search Strategy

For each SR, the manufacturer carried out electronic database searches, accompanied by further searches that included hand searching of selected conference proceedings. A summary of the sources searched for each review is presented in Table 5 of the ERG report (see the "Availability of Companion Documents" field). The ERG notes that for both SRs, searches of the electronic databases were updated on 28th February 2012, using a date restriction of 2011 to present.

Within the manufacturer's submission (MS), the manufacturer provided details of the terms used to search each electronic database. The search strategies included terms for atrial fibrillation (AF), relevant pharmacological interventions and study design. The ERG notes that search terms for the identification of both randomised controlled trials (RCTs) and SRs were included in the RCT evidence SR. In addition, the ERG notes that the RCT evidence SR included search terms for clopidogrel, vitamin K antagonists in addition to warfarin, as well as edoxaban and betrixaban (two new direct factor Xa inhibitors). The ERG notes that edoxaban and betrixaban do not currently have UK marketing authorisation in the indication that is the focus of this STA. Consequently, edoxaban and betrixaban were not included in the final scope for this STA issued by NICE. However, the ERG notes that no studies that focused on the interventions of clopidogrel, edoxaban or betrixaban were included in the MS.

The ERG also notes that for both of the manufacturer's SRs, search terms for atrial flutter were included in the electronic database search strategies. The ERG considers this to be acceptable as there is known to be an association between atrial flutter and AF; therefore, studies indexed as atrial flutter may also report on AF. Furthermore, only those studies reporting on AF were included at the study selection stage; the ERG considers this to be appropriate based on the final scope issued by NICE for this STA.

Because of time constraints for the completion of this report, the ERG has been unable to fully validate the manufacturer's searches and confirm the results. However, the ERG considers that the manufacturer's searches were comprehensive and the search strategies used for each SR were appropriate. In addition, the ERG is not aware of any relevant studies that have been missed by the manufacturer's search.

Inclusion/Exclusion Criteria Used in Study Selection

The manufacturer provided details of the inclusion and exclusion criteria applied to each SR (see Tables 6 and 7 of the ERG report). In addition, the manufacturer presented justifications for any deviations from the PICO (Population, Intervention, Comparators, Outcomes) specified by NICE in the final scope (Tables 6 and 7 of the ERG report).

The manufacturer has deviated from the final scope issued by NICE for this STA; the manufacturer has included aspirin as an additional comparator in patients unsuitable for vitamin K antagonist (VKA) therapy. In addition, studies for either SR were not filtered for the outcomes of transient ischemic attack (TIA) and health-related quality of life (HRQoL).

The ERG also notes that for the non-RCT evidence SR a language restriction was imposed. This limited the results of the review to studies published in English. The manufacturer reported that based on the language restriction, only one study was excluded from the non-RCT evidence SR. However, details of the excluded study were not provided in the MS, therefore, the ERG is unable to comment on the potential impact of the excluded study.

Cost-Effectiveness

A systematic review of the cost-effectiveness literature was carried out by the manufacturer. The objective of the manufacturer's review was to identify economic evaluations of interventions for the prevention of stroke and/or systemic embolism (SE) in adult patients with AF. Standard databases (National Health Service Economic Evaluation Database [NHS EED], Embase, EconLit, Medline In-Process & Other Non-Indexed Citations and OVID MEDLINE) were searched, from 1990 until 12th December 2011. In addition hand-searches of: manufacturer databases, the Cost-Effectiveness Analysis (CEA) Registry, conference proceedings and health technology assessment (HTA) submissions to the National Institute for Health and Clinical Excellence (NICE), were carried out. The ERG notes that the search terms used were reasonable and both inclusion and exclusion criteria were explicitly stated; the ERG considers it unlikely that relevant publications were excluded.

Number of Source Documents

Clinical Effectiveness

- Two randomised controlled trials (RCTs) were included in the review.
- Three RCTs were identified as suitable for inclusion in network meta-analysis (NMA) 1

Cost-Effectiveness

- Nine published cost-effectiveness studies were identified by the manufacturer.
- The manufacturer submitted an economic model.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The Evidence Review Group (ERG) report for this technology appraisal was prepared by Biomedical Journals Technology Assessment Group (BMJ-TAG) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Quality Assessment

The manufacturer assessed the ARISTOTLE and AVERROES trials against criteria adapted from guidance for undertaking reviews in health care issued by the Centre for Reviews and Dissemination, as provided in the NICE template for manufacturer/sponsor submission of evidence to the single technology appraisal (STA) process. The ERG independently validated ARISTOTLE and AVERROES, and agrees with the manufacturer's assessments. The ERG considers both ARISTOTLE and AVERROES to be well-designed randomised controlled trials (RCTs). The ERG acknowledges that there was an imbalance in treatment discontinuations between the treatment groups in each of the RCTs (fewer discontinuations with apixaban in both RCTs) and notes that the manufacturer has used an intention to treat (ITT) analysis to report the results of each study. The ERG considers the manufacturer's approach to data analysis to be appropriate.

Summary and Critique of Submitted Clinical Effectiveness Evidence

The manufacturer presents data for two RCTs, ARISTOTLE and AVERROES, in the clinical effectiveness section of the manufacturer's submission (MS). The ERG considers that only ARISTOTLE met the inclusion criteria for this STA based on the final scope issued by NICE; only ARISTOTLE will be discussed in further detail below. Details and results of AVERROES are presented in Appendix 9.3 of the ERG report (see the "Availability of Companion Documents" field).

Description of ARISTOTLE Trial

ARISTOTLE was an international, multicentre, randomised double-blind phase III trial comparing the clinical efficacy and safety of apixaban with warfarin (vitamin K antagonist, VKA). The patient population of ARISTOTLE had atrial fibrillation (AF) and at least one additional risk factor for stroke. The primary objective of ARISTOTLE was to determine whether apixaban was non-inferior to warfarin (international normalised ratio [INR] target range 2.0–3.0) for the combined end point of stroke and systemic embolism (SE).

See Section 4 of the ERG report for more information on the ARISTOTLE trial; including statistical approaches, summary statement and summary of results.

Description and Critique of Network Meta-analysis

As a result of the absence of head-to-head trials, the manufacturer carried out two network meta-analyses (NMAs). The aim of these NMAs was to compare apixaban with dabigatran and rivaroxaban, as specified in the final scope issued by NICE. NMA 1 consisted of patients suitable for treatment with warfarin and compared apixaban, warfarin, dabigatran and rivaroxaban. NMA 2 was reported in the MS to be in a population of patients unsuitable for vitamin K antagonist (VKA) therapy and compared apixaban, dabigatran, rivaroxaban and aspirin. In the MS, the manufacturer stated that although aspirin was not included in the NICE final scope it remained a relevant comparator in VKA unsuitable patients. The manufacturer’s rationale for this was that aspirin is recommended in clinical guideline 36 (CG36) for patients at moderate to high risk of stroke or SE who are unsuitable for VKA therapy. In addition, the manufacturer stated that aspirin is widely used in clinical practice in England and Wales.

Methods

A total of three RCTs were identified as suitable for inclusion in NMA 1; these are detailed in Section 4.4.3 of the ERG report.

For each outcome of interest, event rates from each RCT were used in the NMA to calculate hazard ratios (HRs). The event rate was defined as the total number of events across all patients, divided by the total patient-years exposed. The ERG notes that if the event rate was not reported in published sources the manufacturer estimated event rates from the number of patients experiencing an outcome. The ERG is unable to provide any comment on the likely impact of this calculation as the true event rates are unknown. It is thus impossible to establish whether the calculated event rate could be over or under estimating the true event rate. However, the manufacturer reported that this method of calculating event rates accurately predicted event rates in the studies where data were available for both event rates and the number of patients with each event.

The manufacturer used a Bayesian Markov Chain Monte Carlo simulation in WinBUGS to conduct the NMA. In the MS, the manufacturer reported that both fixed and random effects models were fitted to the data; the model with the best fit was chosen for the reporting of the results.

Model fit was determined using the deviance information criterion (DIC) and residual deviance for each outcome assessed. The manufacturer reported that there was little difference in model fit between the fixed and random effects models and all outcomes were reported using a fixed effects model. The manufacturer's rationale for the use of a fixed rather than random effects model was built around the small number of studies in the network (three studies). The manufacturer considered that as a result of the small number of included studies, a random effects model would produce poor estimates of the variation in between-study treatment effects. The ERG considers the manufacturer's use of a fixed effects model to be a reasonable choice given the limited data set.

See Section 4 of the ERG report for more information on clinical effectiveness analysis.

Cost-Effectiveness

The manufacturer constructed a Markov model to evaluate the long- and medium-term consequences of apixaban for the prevention of stroke or SE in AF patients. The model captured the clinical and economic consequences of treatment by modelling the movement of patients between discrete health states over a lifetime time horizon.

Model Structure

The Markov model submitted by the manufacturer consisted of 18 health states, including the absorbing state of death. Patients transitioned between health states in cycles of 6 weeks with only one clinical event permitted per cycle. The ERG notes that, given the influence of individual patient characteristics on outcomes in AF, a discreet event simulation rather than a Markov cohort modelling approach may have been more appropriate. However, the ERG acknowledges that a well-constructed Markov model may be sufficient to capture the mean differences in costs and consequences associated with prophylactic treatments in AF. Furthermore, the ERG notes that the use of Markov modelling techniques is consistent with previous novel oral anticoagulant (NOAC) HTA submissions. The model structure for patients on first-line therapy is displayed in Figure 3 of the ERG report. The model structure for patients on second-line therapy is shown in Figure 3 of the ERG report.

Model Validation and Face Validity Check

The manufacturer stated that the model was assessed for internal (verification) and external (validation) validity. Verification was carried out by two independent economists and used extreme value analysis to identify any flawed algorithms or irregularities. Validation was carried out by assessment of the face validity of the model with clinicians and comparison of the model results against published results.

Sensitivity Analysis

In support of the apixaban submission, the manufacturer carried out probabilistic sensitivity analyses (PSAs), deterministic sensitivity analyses, and scenario analyses.

Probabilistic Sensitivity Analyses

The sensitivity of the model to parameter uncertainty while not accounted for in the base case model results has been explored in probabilistic sensitivity analyses. Parameters were assigned a probability distribution from which estimates were simultaneously sampled for 2,000 runs. Table 61 of the ERG report summarises the type of distribution used for each group of parameters considered within the sensitivity analyses; Figures 5 and 6 and Table 62 of the ERG report present the probabilistic results.

Deterministic Analysis

Within the deterministic sensitivity analyses, the manufacturer assessed the univariate sensitivity of the model to a total of 117 parameters. Each parameter was alternately assigned a low and high value estimated from the 95% confidence intervals associated with that parameter; where confidence intervals were not available or could not be derived, variation was assumed to be either 10% or 25% of the mean. Figures 7 to 10 of the ERG report present the deterministic sensitivity analysis results for the 13 most influential parameters in each comparison.

Scenario Analysis

In total, the manufacturer carried out 19 scenario analyses (in the VKA suitable population) around various model assumptions. Table 63 of the ERG report gives the details of each scenario analysis carried out. The results of each analysis with respect to impact on the base case incremental cost-effectiveness ratio (ICER) are displayed in Figure 11 of the ERG report; impact is assessed by percentage change from the base case ICER (for apixaban versus each comparator). The majority of scenario analyses decrease the base case ICER (apixaban versus comparator), suggesting that the assumptions of the base case model were conservative (i.e., any bias was likely to be against apixaban).

See Sections 5 and 6 of the ERG report for more information on methods of cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions on Cost-Effectiveness

Availability and Nature of Evidence

The Committee agreed with the Evidence Review Group (ERG) that the general modelling approach was reasonable and consistent with other analyses of atrial fibrillation treatments.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee concluded that although the general modelling approach was appropriate, weaknesses included the assumption that whether a

person experienced a ischaemic stroke or systemic embolism was treatment related, and there is currently insufficient evidence to support the assumption in the model that the severity of an ischaemic or haemorrhagic stroke was dependent on the specific anticoagulant agent they had received.

The Committee was concerned that there was considerable uncertainty surrounding the relative treatment effects and cost-effectiveness of apixaban, rivaroxaban and dabigatran arising from differences in the baseline characteristics of the people included in the trials and the relative treatment effects attributed to the individual anticoagulants that informed the network meta-analysis. The Committee concluded that there was insufficient evidence to distinguish between the cost-effectiveness of apixaban, dabigatran and rivaroxaban at this time.

Incorporation of Health-Related Quality-of-Life Benefits and Utility Values

The Committee noted that ARISTOTLE had not assessed health-related quality of life and that the utility values used in the manufacturer's model were identified through a systematic review. The Committee questioned whether the manufacturer's assumption of a permanent utility decrement following a myocardial infarction was appropriate. However, it accepted the views of the clinical specialists that disutility following a myocardial infarction would not be expected to change substantially after 6 months. The Committee concluded that the utilities used in the model were appropriate.

Have Any Potential Significant and Substantial Health-Related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

No health-related benefits were identified that were not included in the economic model.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost-Effective?

Apixaban is recommended as an option for all people with nonvalvular atrial fibrillation within its marketing authorisation. No specific groups of people for whom the technology is particularly cost-effective were identified.

What Are the Key Drivers of Cost-Effectiveness?

The Committee noted that only one of the sensitivity analyses performed by the ERG (in which alternative second-line treatments rather than aspirin were considered, see 3.31 of the original guideline document) influenced the results substantially. The Committee accepted the ERG's comment that this analysis should be interpreted with caution because the main driver of the incremental cost-effectiveness ratio (ICER) was discontinuation rates on first-line treatment.

Most Likely Cost-Effectiveness Estimate (Given as an incremental cost-effectiveness ratio [ICER])

The Committee concluded that apixaban had been shown to be cost-effective compared with warfarin, the most plausible ICER being less than £20,000 per quality-adjusted life-year (QALY) gained.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, assessment report and the appraisal consultation document (ACD) and were provided with the opportunity to appeal against the final appraisal determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated for each recommendation.

The Appraisal Committee considered clinical and cost-effectiveness evidence and a review of this submission by the Evidence Review Group. For clinical effectiveness, two randomised controlled trials were the main source of evidence. For cost-effectiveness, nine published cost-effectiveness studies and the manufacturer's model were considered.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation

Potential Harms

The summary of product characteristics lists the following adverse reactions for apixaban: epistaxis (nosebleed), contusion (bruising), haematuria (blood in urine), haematoma, eye haemorrhage, and gastrointestinal haemorrhage.

For full details of adverse reactions and contraindications, see the summary of product characteristics available at http://emc.medicines.org.uk/ .

Qualifying Statements

Qualifying Statements

- This guidance represents the views of the National Institute for Health and Clinical Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

- The Secretary of State and the Welsh Assembly Minister for Health and Social Services have issued directions to the National Health Service (NHS) in England and Wales on implementing National Institute for Health and Clinical Excellence (NICE) technology appraisal guidance. When a NICE technology appraisal recommends use of a drug or treatment, or other technology, the NHS must usually provide funding and resources for it within 3 months of the guidance being published. If the Department of Health issues a variation to the 3-month funding direction, details will be available on the NICE website. When there is no NICE technology appraisal guidance on a drug, treatment or other technology, decisions on funding should be made locally.
- The technology in this appraisal may not be the only treatment for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation recommended in NICE guidance, or otherwise available in the NHS. Therefore, if a NICE technology appraisal recommends use of a technology, it is as an option for the treatment of a disease or condition. This means that the technology should be available for a patient

who meets the clinical criteria set out in the guidance, subject to the clinical judgement of the treating clinician. The NHS must provide funding and resources when the clinician concludes and the patient agrees that the recommended technology is the most appropriate to use, based on a discussion of all available treatments.

- NICE has developed tools to help organisations put this guidance into practice (listed below). These are available on the NICE website (http://guidance.nice.org.uk/TA275).
  - A costing statement explaining the resource impact of this guidance
  - Audit support for monitoring local practice

Implementation Tools

Audit Criteria/Indicators

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Clinical Excellence (NICE). Apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation. London (UK): National Institute for Health and Clinical Excellence (NICE); 2013 Feb. 44 p. (Technology appraisal guidance; no. 275).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Feb

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Clinical Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Dr Jane Adam (*Chair*), Department of Diagnostic Radiology, St George's Hospital; Professor Iain Squire (*Vice-Chair*), Consultant Physician, University Hospitals of Leicester; Professor A E Ades, Professor of Public Health Science, Department of Community Based Medicine, University of Bristol; Dr Jeremy Braybrooke, Consultant Medical Oncologist, University Hospitals Bristol NHS Foundation Trust; Dr Gerardine Bryant, General Practitioner, Heartwood Medical Centre, Derbyshire; Mr Andrew England, Lecturer in Medical Imaging, NIHR Fellow, University of Liverpool; Professor Jonathan Grigg, Professor of Paediatric Respiratory and Environmental Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University London; Dr Brian Hawkins, Chief Pharmacist, Cwm Taf Health Board, South Wales; Dr Peter Heywood, Consultant Neurologist, Frenchay Hospital; Dr Sharon Saint Lamont, Head of Quality and Innovation, North East Strategic Health Authority; Dr Ian Lewin, Consultant Endocrinologist, North Devon District Hospital; Dr Louise Longworth, Reader in Health Economics, HERG, Brunel University; Dr Anne McCune, Consultant Hepatologist, University Hospitals Bristol NHS Foundation Trust; Dr Alec Miners, Lecturer in Health Economics, London School of Hygiene and Tropical Medicine; Ms Sarah Parry, CNS Paediatric Pain Management, Bristol Royal Hospital for Children; Ms Pamela Rees, Lay Member; Dr Ann Richardson, Lay Member; Dr Paul Robinson Medical Director, Merck Sharp & Dohme; Ms Ellen Rule, Programme Director, NHS Bristol; Dr Peter Sims, General Practitioner, Devon; Mr David Thomson, Lay Member; Dr John Watkins, Clinical Senior Lecturer/Consultant in Public Health Medicine, Cardiff University and National Public Health Service Wales; Dr Olivia Wu, Reader in Health Economics, University of Glasgow

Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Clinical Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Edwards SJ, Hamilton V, Trevor N, Nherera L, Karner C, Thurgar E. Apixaban for the prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation: a single technology appraisal. BMJ-TAG, London (UK): 2012. Electronic copies: Available in

Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site .

- Apixaban for preventing stroke and systemic embolism in nonvalvular atrial fibrillation. Costing statement. London (UK): National Institute for Health and Clinical Excellence (NICE); 2013 Feb 27. 6 p. (Technology appraisal 275). Electronic copies: Available in PDF from the NICE Web site .
- Apixaban for preventing stroke and systemic embolism in nonvalvular atrial fibrillation. Clinical audit tool. London (UK): National Institute for Health and Clinical Excellence (NICE); 2013 Mar 28. 7 p. (Technology appraisal 275). Electronic copies: Available from the NICE Web site .

Patient Resources

The following is available:

- Apixaban for preventing stroke and embolism in people with atrial fibrillation. Information for the public. London (UK): National Institute for Health and Clinical Excellence (NICE); 2013 Feb. 6 p. (Technology appraisal 275). Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on April 26, 2013.

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